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EXAMINER	
AKHAVAN, RAMIN	

ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

4/18/2005 RA

Office Action Summary	Application No.	Applicant(s)	
	10/026,331	HITOSHI ET AL.	
	Examiner	Art Unit	
	Ramin (Ray) Akhavan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) *1-7 and 42-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *07/30/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-52 are pending in this application. Acknowledgment is made of a response, filed 01/18/2005, thereby electing claims 8-41 to be examined. Furthermore, receipt is acknowledged of preliminary amendments to the specification inserting sequence identifiers for Figures 4 and 29.

Election/Restrictions

Applicant's election with traverse of Group II (claims 8-40) is acknowledged. The traversal is on the ground(s) that there is no substantial search burden to examine Groups I-VII. This is not found persuasive because as stated previously, the groups I-VII encompass patentably distinct processes, where each process encompasses biologically distinct modalities and action steps. Applicant does not appear to disagree that the methods are patentably distinguishable.

As to search burden, there is a substantial undue burden to examine the distinct inventions together. For example, where a method is directed to *in vivo* treatment (e.g., groups III-VII) the action steps necessary for *in vivo* administration are simply not required for *in vitro* cellular or cell-free assays. Therefore, searching for a particular action step the former groups will not yield the action steps in the latter (e.g., the search results for *in vitro* will not yield the action steps for *in vivo* processes, and vice versa). Furthermore, each of the *in vivo* methods inhere materially different components/elements as well as require different action steps. For example, a search for the step of administering antisense to a subject would not yield results comprising a step of administering an antibody.

Moreover, the modalities involved for each *in vivo* method would require different obstacles to be traversed. For example, in administering nucleic acids there are concerns with target delivery, cell uptake, unpredictable expression levels, etc. In addition, host of different factors are attendant to a method of administering peptides or antibodies (e.g., immunotoxicity, delivery to target cells, dose-response related to adverse outcomes, etc.).

In sum, there is an undue search burden to examine the patentably distinct inventions of groups I-VII. The restriction requirement is still deemed proper and is therefore made FINAL.

Claim Objections

Claims 8, 11, 14, 16, 31-32 and 41 are objected to because of the following informalities: Claims 8 and 41 recite the term "MRE11" without providing a definition of the corresponding term (i.e., meiotic recombination 11). In addition, claim 41 recites the term "SAK" without first providing the corresponding definition.

Claim 11 recites the term "substrate", but would be more precise if the article "a" is inserted before "substrate". Similarly, claim 16 would be more precise if the article "a" is inserted before the term "ligand".

Claim 14 would be more precise if the term "MRE11" is inserted before the term "polypeptide".

Claims 31 and 32 recite the phrase, "the cancer cell is p53 null" and "p53 wild-type". The claims would be more precise if the article "a" is inserted before the term "p53" in each case, and the term "cell" is inserted after the terms "mutant" and "wild-type" respectively. In this way

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

1. **Claims 8-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

Claim 8 recites the limitation "the functional effect", which lacks sufficient antecedent support.

In addition, claim 41 recites the limitation "the SAK polypeptide", which lacks sufficient antecedent support. Furthermore, claim 41 recites the term "fragment thereof" which does not appear to be particularly defined in the specification. It is unclear what sequence(s) the limitation "fragment thereof" encompasses. In other words, the claim is vague and definite as to the boundaries that define "fragment". As such the claim's metes and bounds are indeterminable.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

2. **Claims 8-10, 12, 14-15, 17, 19, 23-29, 35-36 and 38-40 are rejected under 35 U.S.C. 102(e) as being anticipated by Young (US 2002/0115057; See entire document).**

The claims are generally drawn to a screening assay for compounds that affect MRE11 protein functionality in any manner. More particularly, the limitation "MRE11 polypeptide" is interpreted as broadly as reasonable to encompass any polypeptide having "about 60%" identify to amino acids that are encoded by an MRE11 nucleotide sequence – SEQ ID NO: 1. (See, Specification, p. 8, top). In other words, as drafted, the claim is not delimited to the full length MRE11 protein sequence encoded by SEQ ID NO: 1 (or protein consisting of the amino acid sequence of SEQ ID NO: 2). Furthermore, "about" is interpreted as broadly as reasonable to mean an identity somewhere around 60%, but said 60% is not necessarily the minimum.

Moreover, claims 1 and 35 are directed to *any* amino acid or nucleic acid sequence respectively of SEQ ID NO: 2 and SEQ ID NO: 1 (i.e., amino acid and nucleic acid sequence of human MRE11). This interpretation is proper, because the claims delimit the term "sequence" with an indefinite article (i.e., "an" in claim 1; "a" in claim 35).

Therefore, the claims are actually directed to sequences that correspond to *any* of at least 25 amino acids over the entire span of SEQ ID NO: 2 (or sequences encoding said amino acids, i.e., SEQ ID NO: 1). In addition, the limitation "functional effect" is also extremely broad and is interpreted to mean any *in vitro* or *in vivo* MRE11 polypeptide activity. (See, Specification, p. 8, l. 20). Furthermore, the limitations "physical" and "chemical" are not particularly limiting, because the limitations can be interpreted to be mutually inclusive (e.g., chemical can be physical and vice versa). The specification does not exclusively delimit the terms "physical" and "chemical". As such chemical can reasonably be interpreted to include biochemical. For example, modulating gene expression levels has a physical effect in the sense that more or less protein is present in a cell and chemical in that the mRNA under goes biochemical reactions (e.g., translation to protein).

In addition, the limitation "small organic molecule" is interpreted as broadly as possible to include chemotherapeutic agents (e.g., drugs). Further, the limitation "circular" (claim 40) is interpreted as broadly as reasonable, in light of a lack of further clarification of this term in the specification. Therefore any peptide can form a loop, such as in forming its secondary structure (e.g., disulfide bonds).

Young generally teaches a process for identifying anti-cancer therapeutic compounds using cancer gene sets. More particularly, the reference teaches that the screening for a compound comprises the steps of "(a) contacting a compound with a cell containing a polynucleotide comprising a nucleotide sequence...of SEQ ID NO: 1-2276...under conditions where the polynucleotide is expressed [i.e., polypeptide], and (b) determining a change in expression of ... said [protein]...wherein a change in expression is indicative of anti-neoplastic

activity." (See, ¶ 0029). The references discloses SEQ ID NO: 1155, which has over 90% identity to the whole sequence of the claimed SEQ ID NO: 1. (See, attachment, Appendix A; depicting % identity matches for Result No. 4, ID NO: 1155, versus instant SEQ ID NO: 1). Therefore, the disclosed sequence meets the limitation set forth in either claim 8 or claim 35.

The compound can be a "chemical agent" (e.g., implicate chemosensitivity of cells). (e.g., p. 3, ¶¶ 0036, 0048-49). The reference teaches that the assay can be used to determine whether a test compound is anti-neoplastic. If a compound is anti-neoplastic, in the context of the protein encoded by SEQ ID NO: 1155, then the cancer cells do not proliferate, i.e., decreased growth. (e.g., ¶ 0049).

RNA is obtained from eukaryotic host cells (claim 14) so as to measure expression levels (i.e., *in vitro*). (e.g., ¶ 0120). The host cells can be cancer cells, more particularly lung cancer cells (claims 27 to 29). (e.g., ¶¶ 0022, 0044-0047, 0069-0070).

In addition, Young teaches that in contacting cancer cells with a test compound, the compound can be an antibody or a polypeptide. (e.g., ¶¶ 0099, 0101, bridging to p. 10). The reference also teaches that there is a correlation between the RNA levels and the DNA copy number, depending on the form of cancer. Furthermore, an increased RNA level can indirectly measure the amount of DNA, i.e., "DNA amplification" (claim 20). (e.g., ¶¶ 0103-0107). Put another way, an increase in the copy number of a DNA in a cell (i.e., DNA synthesis) results in increased mRNA, further resulting in increased protein production, thereby altering the anti-neoplastic activity (i.e., proliferation). In sum, Young anticipates the rejected claims.

3. **Claims 8-12, 14-17, 19, 23-30, 34-36 and 38-40 are rejected under 35 U.S.C. 102(e) as being anticipated by Morris et al. (US 2002/0182586; See entire document).**

The claims are interpreted consonant with the interpretations stated above. Additional claims delimit the encoded protein (e.g., MRE11) as being recombinant, the cancer cell is HeLa cell, or a p53 null cancer cell, the screening assay further measures a substrate or ligand binding to the MRE11 protein and the candidate compound is an antisense molecule.

Morris et al. teach a method of screening drug candidates comprising providing a cell that expresses a carcinoma associate (CA) gene and also inhibiting cell proliferation. (e.g., ¶¶0007-8). The methods of screening include screening a bioactive agent capable of binding to a CA protein (CAP). (e.g., ¶ 0010). Further, the method of screening is for agents capable of modulating the activity of a CAP, including as said activity relates to cell proliferation. (e.g., ¶¶ 0011, 0191). The reference teaches that CAPs can be encoded by the nucleic acid sequences as depicted in Table 1, which discloses SEQ ID NO: 1223, whereby said sequence shares over 97% identity with instant SEQ ID NO: 1. Therefore, the reference teaches a nucleic acid sequence that encodes a polypeptide having amino acids that share about 60% identity with SEQ ID NO: 2. (See, attachment, Appendix A; depicting % identity matches for Result No. 1, ID NO: 1223, versus instant SEQ ID NO: 1). Furthermore, the protein encoded by said DNA sequence can be a "recombinant protein". (e.g., ¶¶ 0026, 0080). Hereinafter, CAP should be construed as applying to the particular sequence, SEQ ID NO: 1223 (or instant SEQ ID NO:2) within the context of the base claims.

Furthermore, depending on the cancer, the reference teaches that DNA copy numbers can be increased/decreased. (e.g., ¶ 0206).

Therefore, measuring RNA expression levels will indirectly measure DNA synthesis (e.g., more copies of DNA correlating to higher expression levels, in the context of the anti-cancer effects of the test compound). In addition, the reference teaches a host of cancer cells that can be utilized in the screening methods, including lung cancer. (e.g., ¶¶ 0021-22). More particularly, appropriate host cells include HeLa cells, which do not express p53 and is a transformed cell line (i.e., p53 null; claim 31). (e.g., ¶ 0077 bridging to p. 9).

The candidate agent to be screened can be a nucleic acid molecule or an antisense molecule. (e.g., ¶ 0027, middle; ¶ 0201). Furthermore, candidate agents can be peptides as well as antibodies (e.g., ¶¶ 0194, 0209). Furthermore, agents are screened to determine whether they enhance or inhibit CAP activity. (e.g., ¶¶ 0193, 0195). The candidate agent can also be a substrate or ligand that binds CAP, whereby binding is measured in the screening assay. (e.g., ¶¶ 0189. 0200-202). In sum, Morris et al. anticipate the rejected claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ray Akhavan whose telephone number is 571-272-0766. The examiner can normally be reached between 8:30-5:00, Monday-Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD, can be reached on 571-272-0781. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

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Respectfully submitted,

Ray Akhavan/AU 1636

GERRY LEFFERS
PRIMARY EXAMINER